AUSTRALIAN PRODUCT INFORMATION - SOLUVIT® N (THIAMINE NITRATE, RIBOFLAVINE SODIUM PHOSPHATE, NICOTINAMIDE, PYRIDOXINE HYDROCHLORIDE, SODIUM PANTOTHENATE, SODIUM ASCORBATE, BIOTIN, FOLIC ACID, CYANOCOBALAMIN)

1 NAME OF MEDICINE

Thiamine nitrate
Riboflavine sodium phosphate
Nicotinamide
Pyridoxine hydrochloride
Sodium pantothenate
Sodium ascorbate
Folic acid
Biotin
Cyanocobalamin

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Soluvit N is a lyophilised, sterile, yellow mixture of water-soluble vitamins for intravenous infusion.

Active Ingredients	Quantity in one vial	1 mL of reconstituted Soluvit N contains:
Thiamine nitrate	3.1 mg	0.31 mg
Riboflavine sodium phosphate (corresponding to Vitamin B_2 3.6 mg)	4.9 mg	0.49 mg
Nicotinamide	40 mg	4.0 mg
Pyridoxine hydrochloride (corresponding to Vitamin B_6 4.0 mg)	4.9 mg	0.49 mg
Sodium pantothenate (corresponding to Pantothenic acid 15.0 mg)	16.5 mg	1.65 mg
Sodium ascorbate (corresponding to Vitamin C 100 mg)	113 mg	11.3 mg
Biotin	60 micrograms	6.0 micrograms
Folic acid	400 micrograms	40 micrograms
Cyanocobalamin	5.0 micrograms	0.5 micrograms

For the full list of excipients, see Section 6.1 List of excipients.

3 PHARMACEUTICAL FORM

Powder for Injection, vial.
A yellow, porous freeze-dried cake.
Osmolality in 10 mL of water: approx. 490 mOsm/kg water
pH in 10 mL of water: 5.8

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Soluvit N is intended as a supplement in intravenous nutrition in order to meet the daily requirements of the water-soluble vitamins in adults, adolescents, children and infants. Fat-soluble vitamins should also be administered to patients receiving prolonged parenteral nutrition.

4.2 Dose and method of administration

Soluvit N may be added to parenteral nutrition admixtures containing carbohydrates, lipids, amino acids, electrolytes, and trace elements, provided that compatibility and stability have been confirmed.

Soluvit N must not be given undiluted. The reconstituted Soluvit N should be added to the infusion solution under sterile conditions, immediately before the start of the infusion and used within 24 hours. Clear admixtures (e.g. glucose solution or Water for Injections) containing Soluvit N should be protected from light.

The reconstituted mixtures with Vitalipid, Intralipid and SMOFlipid must be added under sterile conditions to Intralipid only. The reconstituted mixtures with Water, Sodium Chloride 0.9% and Glucose are added under sterile conditions to Intralipid or glucose solutions for infusion.

Adults and children weighing 10 kg or more

The recommended daily dosage is the contents of one vial.

The contents of one vial are dissolved by the aseptic addition of 10 mL of one of the following:

1. Vitalipid N Adult/Infant*
2. Intralipid 10%, 20% or 30%# lipid emulsion for infusion
3. Water for Injections
4. Sodium chloride 0.9% injection
5. Glucose solution for infusion
6. SMOFlipid®

*Vitalipid N Adult is only indicated for use in patients aged 11 years and above
Intralipid 30% is not recommended in children

Children and Infants weighing less than 10 kg

Children and infants weighing less than 10 kg should be given 1/10 (1 mL) of the content of one vial per kg body weight per day.

The contents of one vial are dissolved by the aseptic addition of 10 mL of one of the following:

1. Vitalipid N Infant*
2. Intralipid 10% or 20%
3. Water for Injections

4. Sodium chloride 0.9% injection
5. Glucose solution for infusion
6. SMOFlipid®

*The mixture Soluvit N and Vitalipid N Infant is not recommended for those weighing less than 10 kg.

4.3 Contraindications
Known hypersensitivity to any of the components, for example, thiamine or methyl hydroxybenzoate.

4.4 Special warnings and precautions for use
Administering folic acid may obscure pernicious anaemia. The Soluvit N doses recommended are insufficient to correct severe vitamin deficiency states and may be insufficient in patients with markedly increased vitamin requirements. In patients receiving total parenteral nutrition (TPN), routine supplementation with both fat-soluble and water-soluble vitamins is recommended to prevent deficiency states and to obviate the need to speculate on individual vitamin status. Daily vitamin requirements must be calculated to avoid overdosage and toxic effects, especially with regards to vitamins A and D, and particularly in paediatric patients. In patients for whom TPN is continued for prolonged periods (months or years), periodic monitoring of blood vitamin levels should be considered.

To prevent excessive excretion of water-soluble vitamins, and for reasons of safety, daily dosage should be administered over a number of hours. See also the product information for Intralipid, SMOFlipid or Vitalipid N if Soluvit N is dissolved in these products.

Use in hepatic impairment
No data available.

Use in renal impairment
No data available.

Use in the elderly
There have been no specific clinical studies conducted with Soluvit N in the elderly.

Paediatric use
No data available.

Effects on laboratory tests
No effects on laboratory tests have been identified.

4.5 Interaction with other medicines and other forms of interactions
Vitamin B_6 can reduce the effect of levodopa. Folic acid may lower the serum concentration of phenytoin. Other drugs should not be added to Soluvit N dissolved in Intralipid, SMOFlipid or Vitalipid N, due to the possibility of physical incompatibilities (see product information for Intralipid, SMOFlipid and Vitalipid N).

4.6 Fertility, pregnancy and lactation

Effects on fertility

The potential effects of Soluvit N on fertility and general reproductive performance have not been determined.

Use in pregnancy

The requirement of vitamins in pregnant women may be insufficient due to the patient's altered needs. Soluvit N has been administered to pregnant women with no adverse reactions reported.

Use in lactation

The requirement of vitamins in lactating women may be insufficient due to the patient's altered needs.

4.7 Effects on ability to drive and use machines

The effects of this medicine on a person's ability to drive and use machines were not assessed as part of its registration.

4.8 Adverse effects (Undesirable effects)

Allergic reactions including anaphylactic reactions may occur in patients hypersensitive to any component in the preparation, for example, folic acid, methyl hydroxybenzoate or thiamine (frequency not known). There have been rare reports of anaphylactoid reactions following repeated injection of preparations containing thiamine. Flushing, itching or burning of the skin may occur in patients susceptible to the effects of nicotinamide. Evaluable safety data from clinical trials with Soluvit N are limited. Adverse reactions that may be expected based on experience with other water-soluble vitamin compounds administered intravenously include: allergic reactions, including anaphylaxis; dermatological reactions including flushing, erythema, pruritus, and CNS reactions including headache, dizziness, and agitation.

Reporting suspected adverse effects

Reporting suspected adverse reactions after registration of the medicinal product is important. It allows continued monitoring of the benefit-risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions at https://www.tga.gov.au/reporting-problems.

4.9 Overdose

Adverse effects caused by an overdose of water soluble vitamins have been reported and are unlikely to occur when administered as recommended. In cases of suspected overdose, symptomatic and supportive therapy should be instituted as appropriate, and further administration of the product discontinued.

For information on the management of overdose, contact the Poison Information Centre on 131126 (Australia) or 0800 764 766 (New Zealand).

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Mechanism of action
ATC code: B05X C00

Soluvit N is a mixture of water-soluble vitamins in amounts normally absorbed from the oral diet and should have no pharmacodynamic effect besides maintaining the nutritional status in patients requiring home PN. Additional amounts of some vitamins may be needed e.g. surgery, malnutrition, burns to avoid certain diseases caused by deficiency.

Clinical trials
No clinical data is available.

5.2 Pharmacokinetic properties

When infused intravenously the water-soluble vitamins in Soluvit N are utilised in a generally similar way to water-soluble vitamins from an oral diet.

Absorption
No data available.

Distribution
No data available.

Metabolism
No data available.

Excretion
No data available.

5.3 Preclinical safety data

Genotoxicity
Studies with Soluvit N have not been performed to evaluate the genotoxic potential.

Carcinogenicity
Studies with Soluvit N have not been performed to evaluate the carcinogenic potential.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Excipients	Quantity per vial
Glycine	300 mg
Edetate sodium	500 micrograms
Methyl hydroxybenzoate (preservative)	500 micrograms

6.2 Incompatibilities

Soluvit N may only be added to or mixed with other medicinal products for which compatibility has been documented, refer to **section 4.2 - Dose and method of administration**. Please also refer to **section 4.5 - Interactions with other medicines and other forms of interactions** for incompatibilities of the product.

6.3 Shelf life
Approved shelf life: 18 months
The expiry date can be found on the packaging.

6.4 Special precautions for storage
Store below 25°C. Protect from light.

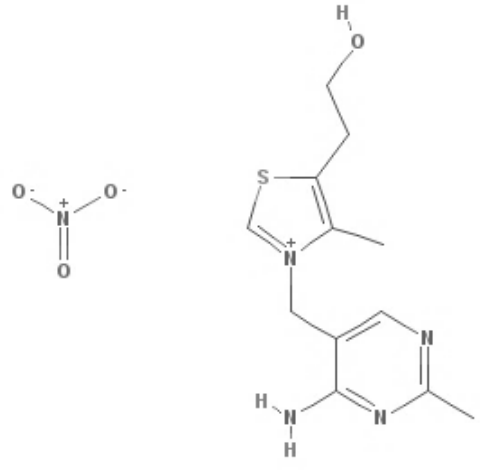
6.5 Nature and contents of container
Soluvit N is a sterile, lyophilised powder containing a mixture of the water-soluble vitamin B_1, vitamin B_2, nicotinamide, vitamin B_6, pantothenic acid, vitamin C, biotin, folic acid, and vitamin B_{12}. Methyl hydroxybenzoate and edetate sodium are included as stabilisers.

Glass vials (Type I)
Stopper for injection vial, chlorobutyl rubber
Vials: box of 10
AUST R 40145

6.6 Special precautions for disposal
In Australia, any unused medicine or waste material should be disposed of in accordance with local requirements.

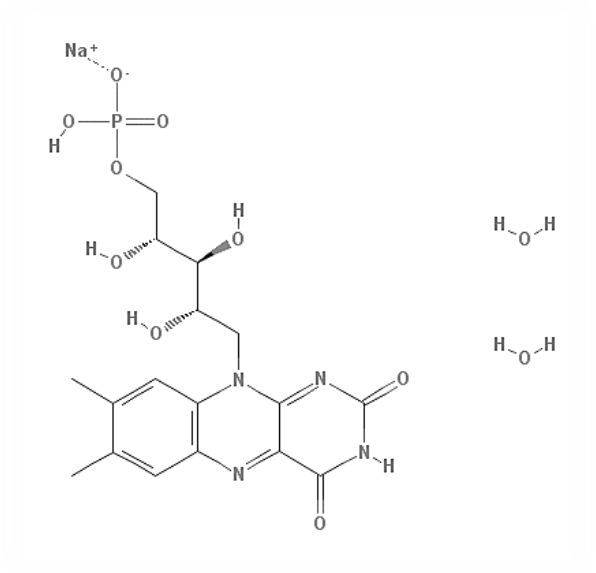
6.7 Physicochemical properties
Chemical structure

Thiamine nitrate



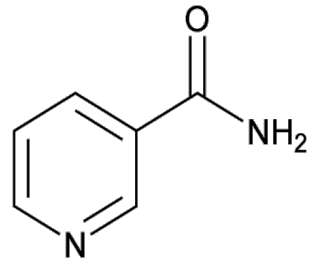
Empirical formula: $C_{12}H_{17}N_5O_4S$
Molecular weight: 327.36
Chemical name: Thiazolium, 3-[(4-amino-2-methyl-5-pyrimidinyl)methyl]-5-(2-hydroxyethyl)-4-methyl-nitrate

Riboflavine sodium phosphate



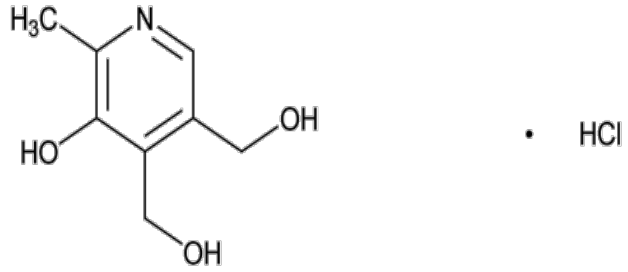
Empirical formula: $C_{17}H_{20}N_4NaO_9P \cdot 2H_2O$
Molecular weight: 514.36
Chemical name: riboflavin 5′-(dihydrogen phosphate), monosodium salt, dihydrate

Nicotinamide



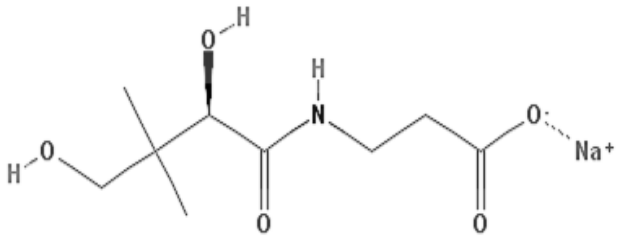
Empirical formula: $C_6H_6N_2O$
Molecular weight: 122.12
Chemical name: 3-pyridinecarboxamide

Pyridoxine hydrochloride



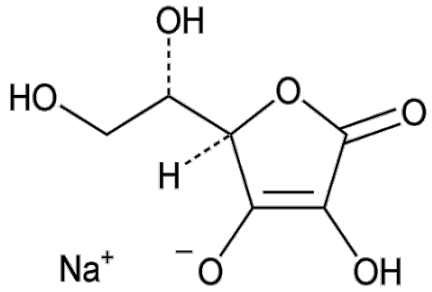
Empirical formula: $C_8H_{11}NO_3 \cdot HCl$
Molecular weight: 205.64
Chemical name: 3,4-pyridinedimethanol, 5-hydroxy-6-methyl-hydrochloride

Sodium pantothenate



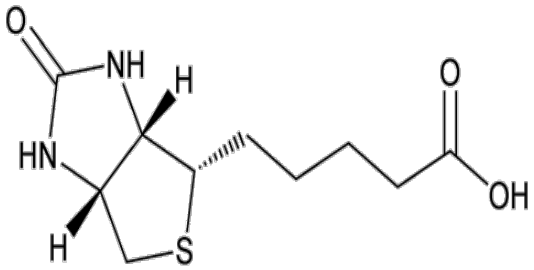
Empirical formula: $C_9H_{16}NNaO_5$
Molecular weight: 241.22
Chemical name: sodium (R)-3-(2,4-dihydroxy-3,3-dimethylbutanamido)propanoate

Sodium ascorbate



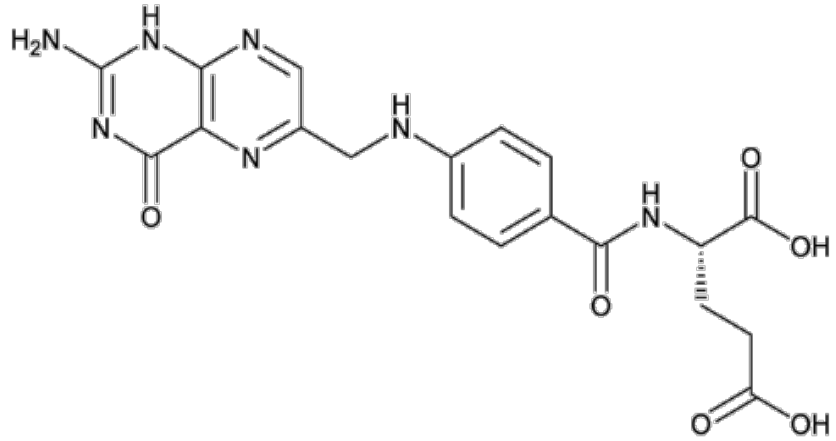
Empirical formula: $C_6H_7NaO_6$
Molecular weight: 198.11
Chemical name: sodium (2R)-2-[(1S)-1,2-dihydroxyethyl]-4-hydroxy-5-oxo-2H-furan-3-olate

Biotin



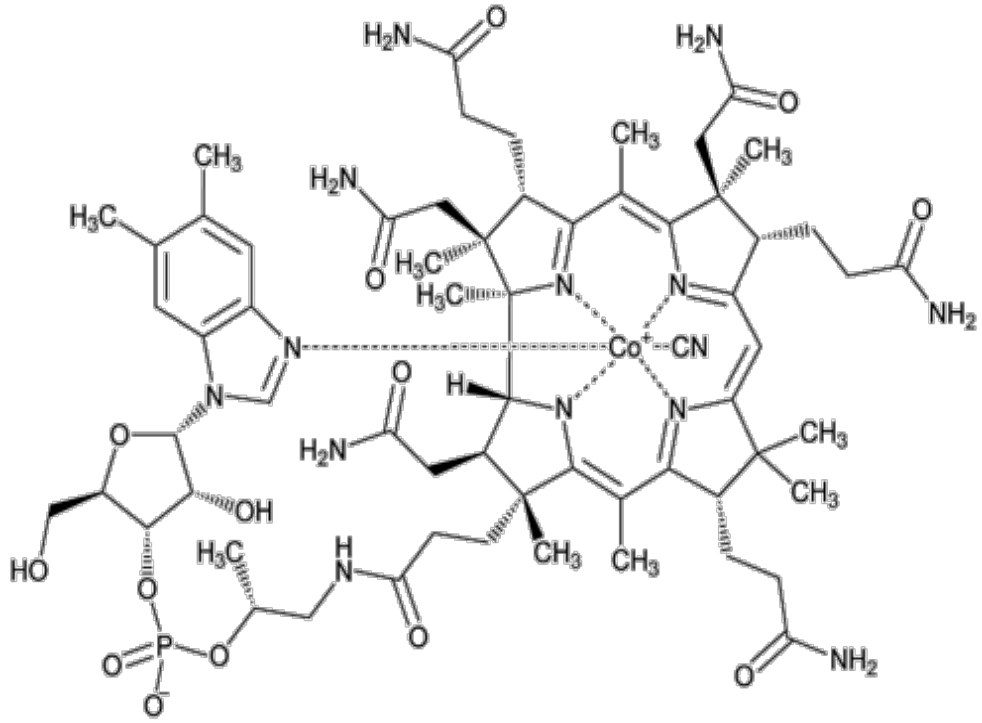
Empirical formula: $C_{10}H_{16}N_2O_3S$
Molecular weight: 244.31
Chemical name: 5-[(3aS,4S,6aR)-2-oxohexahydro-1H-thieno[3,4-d]imidazol-4-yl]pentanoic acid

Folic acid



Empirical formula: $C_{19}H_{19}N_7O_6$
Molecular weight: 441.40
Chemical name: (2S)-2-[[4-[(2-Amino-4-oxo-1H-pteridin-6 yl)methylamino]benzoyl]amino] pentanedioic acid

Cyanocobalamin



Empirical formula: $C_{63}H_{88}CoN_{14}O_{14}P$
Molecular weight: 1355.37
Chemical name: cyanocobalamin

CAS number

Active Ingredient	CAS number
Thiamine nitrate	532-43-4
Riboflavine sodium phosphate	130-40-5
Nicotinamide	98-92-0
Pyridoxine hydrochloride	58-56-0
Sodium pantothenate	867-81-2
Sodium ascorbate	134-03-2
Biotin	58-85-5
Folic acid	59-30-3
Cyanocobalamin	68-19-9

7 MEDICINE SCHEDULE (POISONS STANDARD)

Australia: Not Scheduled
New Zealand: General Sale Medicine

8 SPONSOR

Fresenius Kabi Australia Pty Limited
Level 2, 2 Woodland Way
Mount Kuring-gai, NSW 2080
Australia.
Telephone: (02) 9391 5555

Fresenius Kabi New Zealand Limited
60 Pavilion Drive
Mangere, Auckland 2022
New Zealand.
Freecall: 0800 144 892

9 DATE OF FIRST APPROVAL

21 August 1992

10 DATE OF REVISION

23 October 2018

Summary table of changes

Section Changed	Summary of new information
All	Revised to the new PI format as per TGA requirements
2	Added quantities equivalent in 1ml of reconstituted Soluvit N
3	Added description of powder and dosage form
4.1	Added indications for paediatric use
6.3	Added shelf life of 18 months as per new TGA PI form template
6.5	Added glass type - type I
6.7	Added chemical structure, empirical formula, molecular weight and chemical name for each active ingredient. CAS numbers included.